In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: June 3, 2008

Examiner: Michael L. BORIN
Group Art Unit: 1631
Attorney Docket: 35898

## REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-57, 102, 103 and 155-163 are in this Application. Claims 7, 10-13, 16-23, 37-39, 50-53, 57, 102, 103 and 157 have been withdrawn as being drawn to non-elected species. Claims 1-4, 26, 29-33, 36, 41-46, 155, 156, 158, 159 and 161 have been rejected under 35 U.S.C. §102 and 103. Claims 58-101, 104-154 and 164-171 have been canceled in a previous response. Claims 26-28 and 160 have been cancelled herewith. Claims 1, 2, 6-8, 14-18, 24, 25, 29-31, 34, 35, 44-46, 161 and 162 have been amended herewith.

### *Amendments To The Claims*

Before discussing specific rejections, Applicant wishes to note that the present invention includes the quantitative measurement of at least part of a target, with respect to the type of chemical binding points present on the target and to the distances therebetween. Such measurement is conceptually different than prior methods of studying a target by observing binding of molecules to bind to the target.

In order to provide measurements of a target, the present invention includes the provision of a set of particularly suitable molecules. Such a set has not been taught prior to the instant application. These molecules are referred to as "gauges" in the instant application in order to emphasize their unique suitability for measuring targets, as well as the difference between the present invention and methods previously known in the art.

### *Claim Objections*

The Examiner has objected to claims 34 and 35 under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Specifically, the Examiner has stated that the claims are directed to use of more than one set of gauges whereas the base claim 1 is directed to use of one set of gauges.

Claims 34 and 35 have been amended so as to recite "said set of gauges" instead of "at least said set of gauges". Hence, claims 34 and 35 are directed to use of a set of gauges, as is claim 1.

Applicant believes that the above amendments do not affect the scope of the claims.

Applicant therefore believes to have overcome the Examiner's objection.

*35 U.S.C. §112, 2nd Paragraph Rejections*

The Examiner has rejected claims 1-6, 8, 9, 14, 15, 24-36, 40-49, 54-56, 155, 156 and 158-163 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, the Examiner has cited the following reasons for rejecting the claims:

A. The Examiner has stated that the term "mathematical-chemical space" in claim 1 is vague and indefinite, and that the specification addresses "measurement space", "virtual space", "space of models", "array of spaces, one space for each set of chemical behaviors" and "chemical configuration space", but does not address "mathematical-chemical space". The Examiner has concluded that one of ordinary skills in the art would not be reasonably apprised of the scope of the invention.

Applicant believes that the instant application provides a highly detailed description of a mathematical space for defining chemical structures, and it would therefore be clear to one of skill in the art that the term "mathematical-chemical space" refers to such a space.

Notwithstanding the above, claim 1 has been amended so as to recite "triangle space" instead of "mathematical-chemical space".

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Applicant wishes to note that the specification addresses "triangle space" numerous times.

In addition, claim 1 has been amended so as to more clearly define the triangle space. Thus, claim 1 has been amended to recite:

*"...said triangle space defining all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein said 3-point pharamcophore represents a set of three binding points on a molecule to which a gauge may bind...."*

Applicant therefore believes that the term "triangle space" is clear, and that one of skill in the art would be adequately apprised of the scope of the invention.

The use of the term "3-point pharmacophore" to describe a triangle of chemical binding point types on a molecule to which a gauge may bind is supported, for example, on page 4, line 28, to page 5, line 12, of the instant application.

Applicant believes that the use of the term "triangle space" and the use of the term "3-point pharmacophore" to describe the triangle space are purely cosmetic changes which do not alter the scope of the claim.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

B. The Examiner has stated that the claim addresses "chemical gauges", which are understood as molecules, as well as "geometric substructures" of the gauges, and that a molecule does not have geometric substructures. The Examiner has stated further that a model may be addressed as having a "geometrical substructures", and has requested clearer claim language.

Applicant believes that it is standard practice in the art to refer to a molecule as having a structure, and that a part of said structure of a molecule can therefore be

termed a "substructure". Applicant therefore believes that a molecule can be considered as having a "geometrical substructure".

Notwithstanding the above, Applicant has chosen to amend claim 1 so as to recite a chemical gauge (a molecule) "comprising at least one set of three binding points in a substantially rigid triangular configuration", and to further recite the defining of a "triangular geometric substructure which represents a set of three binding points, each triangular geometric substructure being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices".

Hence, the "triangular geometric substructure" in amended claim 1 describes a feature of a model of a molecule, rather than a feature of a molecule.

Applicant believes that the above amendments do not affect the scope of the claim.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

C. The Examiner has stated that claim 1 recites the broad recitation that only at least 50% of space is spanned, as well as the narrower statement that each point in space is covered by at least 5 distinct gauges, and that a broad limitation together with a narrower limitation is considered indefinite.

Claim 1 has been amended so as to no longer recite the phrase "each point in said space....".

Instead, amended claim 1 recites the number of gauges covering a spanned portion of space within the definition of spanned space. Thus, claim 1 has been amended to recite:

*"...a portion of said space being defined as being spanned if there are at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to each 3-point pharmacophore defined by said portion of said space."*

The description of at least six gauges with a configuration capable of binding to each 3-point pharmacophore defined by a space is supported, for example, on page 4, lines 13-15, of the instant application.

Applicant therefore believes that the elimination of the phrase "each point in said space" does not affect the scope of the claim.

Furthermore, as discussed hereinabove, Applicant believes that the use of the term "3-point pharmacophore" to describe triangle space does not alter the scope of the claim.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

D. The Examiner has stated that the phrase "each point in...space" is not clear.

As described hereinabove, claim 1 has been amended so as to no longer recite the phrase "each point in said space".

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

E. The Examiner has stated that it is not clear whether the claimed invention of claim 1 is directed to an *in silico* method, an *in vitro* method, or combination of the two. The Examiner has requested clearer claim language.

Applicant believes that it would be apparent to one of skill in the art the claimed invention includes both experimental steps (e.g., "assaying said interaction of said gauges with said target") and computational steps (e.g., "analyzing said assay results"), particularly in view of the detailed description of the embodiments of the invention included in the specification.

Notwithstanding the above, Applicant has chosen to amend claim 1 so as to more clearly describe the subject matter thereof. Thus, claim 1 has been amended to recite (emphasis added):

*"A method of obtaining information about a chemically active area of a target molecule, comprising:*

*providing a set of compounds comprising a set of substantially rigid chemical gauges, each of said gauges comprising at least one set of three binding points in a substantially rigid triangular configuration;*

*for each of said gauges, defining at least one triangular geometric substructure which represents a set of three binding points, each triangular geometric substructure being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices;*

*performing a plurality of assays for measuring an interaction of said target with said gauges, each assay measuring an interaction of said target with at least one of said gauges, thereby obtaining a plurality of assay results; and*

*analyzing said assay results using a plurality of said triangular geometric substructures to obtain information about said chemically active area,*

*said set of gauges being selected such that at least 50% of a triangle space is spanned by said gauges,*

*said triangle space defining all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein said 3-point pharmacophore represents a set of three binding points on a molecule to which a gauge may bind; and*

*a portion of said space being defined as being spanned if there are at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to each 3-point pharmacophore defined by said portion of said space."*

Applicant believes that the amended claim language emphasizes the inclusion of both experimental and computational steps. Specifically, the steps "providing a set of compounds" and "performing a plurality of assays" are clearly experimental in

nature, and the steps "for each of said gauges, defining...." and "analyzing said assay results" are clearly computational in nature.

Regarding the above amendment, Applicant wishes to note that the amendment of claim 1 to recite "a set of compounds comprising a set of substantially rigid chemical gauges" broadens the scope of the claims. The amendment is supported, for example, on page 76, lines 3-6, of the instant application, wherein the option of using non-rigid molecules in addition to the substantially rigid gauges is discussed.

Applicant wishes to note further that the passage "performing a plurality of assays..., thereby obtaining a plurality of assay results" in amended claim 1 corresponds to the passage "causing said target to interact...to obtain a plurality of assay results" recited previously. Applicant believes that this amendment does not affect the scope of the claims.

Applicant wishes to note further that the phrase "using a plurality of said triangular geometric substructures" has been added to the passage "analyzing said assay results to obtain information about said chemically active area". Applicant believes that this amendment is purely cosmetic.

Applicant further believes that amending the passage "such that at least 50% of a mathematical-chemical space is spanned by the substantially rigid triangular geometric substructures of said gauges" so as to recite "said set of gauges being selected such that at least 50% of a triangle space is spanned by said gauges" does not affect the scope of the claims.

In view of the above amendment to claim 1, claim 2 has been amended so as to better accord with the claim language of amended claim 1, from which claim 2 depends. Thus, claim 2 has been amended to recite:

*"A method according to claim 1, wherein said set of gauges is selected such that at least 50% of a portion of said triangle space covering the range of distances of between 4 and 8 angstrom is spanned."*

Applicant believes the amendment to claim 2 is purely cosmetic.

Additionally, claims 6-8, which depend from claim 1, have been amended so as to better accord with the claim language of amended claim 1. Thus, claims 6-8 have been amended so as to recite "3-point pharmacophore" instead of "configuration" or "triangular configuration" when referring to a configuration on a target. Similarly, claims 7 and 8 have been amended so as to recite "triangular configuration" instead of "configuration" when referring to a configuration of a gauge.

As discussed hereinabove, the use of the term "3-point pharmacophore" to describe a triangular configuration is supported in the instant application. Furthermore, as claim 1, from which the abovementioned claims depend, describes triangular substructures, it would have been apparent to one of skill in the art that the recited configurations of a gauge, as well as configurations which match configurations of a gauge, referred to a triangular configuration.

Hence, Applicant believes that the abovementioned amendments to claims 6-8 are purely cosmetic.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

F. The Examiner has stated that it is not clear whether the term "binding" in claims 29-31, 44-46 and 161 refers to binding in the course of interaction of gauges with the target (presumably *in vitro*), or to binding in the sense of descriptor of a gauge's ability to interact in "mathematical-chemical space" (presumably *in silico*).

As discussed hereinabove, claim 1 has been amended so as to more clearly distinguish experimental steps from computational steps.

Applicant believes that it would be clear to one of skill in the art that the term "binding" in the cited claims refers to an interaction of a gauge with the target, particularly as claim 1, from which the cited claims depend, clearly refers to an interaction of gauge and target measured by assay (e.g., "...performing a plurality of assays for measuring an interaction of said target with said gauges...."), and the instant application describes binding as an exemplary form of interaction between

gauge and target to be detected by assay (see for example, page 3, lines 4-9; page 29, lines 18-21; and page 30, line 29, to page 31, line 29, therein).

Moreover, claims 44-46 recites "analyzing comprises analyzing successful binding" which clearly refers to the analyzing of assay results recited in claim 1.

In contrast, claim 1 does not refer to an interaction of a gauge with a target in any computational step thereof. Moreover, claim 1 does recite a "target" in a mathematical space, but rather "3-point pharmacophores".

Notwithstanding the above, Applicant has chosen to amend claims 29-31 and 161 so as to emphasize the experimental nature of the binding. Thus, claims 29-31 and 161 have been amended so as to recite "when said target is interacted with said gauges".

Applicant believes that the above amendments are purely cosmetic.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

G. The Examiner has stated with regard to claims 24, 25, 27, 28, 44-46, and 160-162 that in claims addressing plurality of gauges, it is not clear whether the gauges in the set are all of distinct structure.

Claims 27, 28 and 160 have been canceled without prejudice.

Applicant wishes to note that claim 162 does not refer to gauges, and hence, Applicant believes this rejection of claim 162 is erroneous.

It is not entirely clear to Applicant what is meant by the Examiner's phrase "all of distinct structure". However, Applicant believes that it would be readily apparent to one of skill in the art that the recited set of gauges refers to a set of distinct (i.e., non-identical) gauges.

Notwithstanding the above, and in order to further clarify the claim language, Applicant has chosen to amend claims 24, 25 and 44-46 so as to refer to a plurality of "distinct gauges" instead of "gauges".

Applicant believes that the abovementioned amendments are purely cosmetic.

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Applicant wishes to note that claim 161, which depends directly from claim 1, refers to a plurality of gauges only via the phrase "said gauges". Applicant believes that it is clear that the gauges recited in claim 1 refer to non-identical gauges. Thus, for example, claim 1 recites that "for each of said gauges" a triangular geometric substructure is defined, which clearly implies that the gauges of the set are not identical. Moreover, the Examiner has not stated that it is not clear whether the gauges in claim 1 are distinct. Applicant therefore believes that the nature of the gauges in claim 161 is clearly addressed by the claim language of claim 1.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

H. The Examiner has stated that the term "point" in claims 27, 28, 160 and 161 is ambiguous.

As described hereinabove, claims 27, 28 and 160 have been canceled without prejudice, rendering moot the Examiners rejection of these claims.

Furthermore, Applicant wishes to note that the term "point" does not appear in claim 161. Hence, Applicant believes this rejection of claim 161 is erroneous.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

I. The Examiner has stated that claim 8 addresses the result of identifying a configuration that does not match a configuration of a bound gauge, and that it is not clear how, in the absence of further defining of the area to be assayed, one can know that there will be configurations that do not match a configuration of a bound gauge.

Applicant believes that it is within the capabilities of one of skill in the art to determine whether a configuration (e.g., 3-point pharmacophore) will bind to a triangular configuration of a bound gauge, based on the distances of the configurations (e.g., triangle sides) and the chemical properties of the binding types thereof, as such calculations are commonly practiced in the chemical arts. Thus, one

of skill in the art could readily identify a possible configuration as having the property of not matching the triangular configuration of a bound gauge.

Applicant therefore believes that no further defining of the target active area is necessary.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

J. The Examiner has stated that claims 14 and 15 address the result of covering a certain number of chemical binding areas, and that it is not clear how, in the absence of further defining of the area to be assayed, one can know the amount of areas to be discovered by the method prior to applying the method itself.

Claims 14 and 15 relate to a construction of a spatial map of an area on a target, by utilizing the information obtained from a plurality of assay results. The mapped area has at least 4 binding areas according to claim 14, and at least 6 according to claim 15.

The number binding areas mapped by the spatial map is determined by the complexity of the spatial map reconstruction. Thus, for example, a spatial map constructed by combining two triangles sharing a common side (wherein each triangle vertex represents a binding area) will have four binding areas, whereas a spatial map with more binding areas can be reconstructed by combining a larger number of triangles. The mapping of 4 (or 6) binding areas is therefore not a property of the assayed area *per se*, rather it is determined by the complexity of map construction.

Various types of map construction are discussed in detail in the instant application (see, for example, pages 41-45, Section 6.2, therein).

Applicant wishes to note that even chemically active areas of targets generally have at least 10 binding areas (see for example, page 5, lines 6-8, of the instant application), and therefore the reconstruction of a spatial map with at least 4 or 6 binding areas is achievable with a high degree of certainty.

Applicant therefore believes that it would be readily apparent to one of skill in the art how one can construct a spatial map including at least 4 or at least 6 binding areas (as per claims 14 and 15, respectively).

Notwithstanding the above, Applicant has chosen to amend claims 14 and 15 in order to make more clear that the recited number of binding areas refers to a property of the spatial map reconstruction, rather than to a property of the assayed target.

Hence, claims 14 and 15 have been amended so as to recite "said spatial map including...." instead of "said part including....".

Similarly, withdrawn claims 16 and 17 have been amended so as to recite "said spatial map" instead of "said part".

Applicant believes that the abovementioned amendment is purely cosmetic.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

K. The Examiner has stated that claims 29-31 address the amount of gauges that bind with the target and that it is not clear how, in the absence of further defining of the area to be assayed, one can know the amount of gauges that bind with the target prior to applying the method itself.

Gauge sets according to embodiments of the present invention are expected to exhibit a relatively high binding percentage to a target, as the gauge set spans a large percentage (at least 50%) of triangle space. Hence, it is likely that at least some of the gauges in the gauge set will span a portion of triangle space corresponding to the target.

In contrast, sets of compounds described in the prior art comprise substantially rigid compounds which span only a small portion of triangle space. It is therefore likely that a portion of triangle space corresponding to the target is not spanned at all by the set of compounds, thereby reducing the probability of binding.

Moreover, the binding percentage of a gauge set according to embodiments of the present invention may be enhanced further by selected the gauge set according to

appropriate criteria, for example, selecting the gauges such that the portion of triangle space spanned by the gauge set includes the portion of triangle space corresponding to the target.

For example, gauges may be selected based on their resemblance to compounds known to bind to the target or related substances (e.g., many compounds are known in the art to have an affinity towards proteins in general), and/or based on known physical properties of the target (e.g., a net positive or negative charge).

Furthermore, Applicant wishes to note that although it is impossible to know with absolute certainty how many gauges will bind to the target before performing a binding assay, performance of an assay is merely a single step of the method, and does not represent a complete application of the method. Thus, according to the embodiments of claims 29-31, assay results are simply not analyzed if they do not meet the requirements recited in the claims, as low numbers of gauges that interact with the target may reduce the accuracy of the analysis.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

L. The Examiner has stated that claims 47-49 are directed to identifying a certain amount of different configurations, and that it is not clear how, in the absence of further defining of the area to be assayed, one can know the amount of different configurations to be discovered by the method prior to applying the method itself.

As would be apparent to one of skill in the art, the amount of identified configurations is not simply a function of the target being analyzed, but depends largely on the number of gauges which bind the target. As discussed hereinabove (with regard to Item K), the minimal percentage of gauges expected to bind any target is enhanced by the use of a gauge set which spans a large portion of triangle space, as well as by selection of the gauge set to span the portion of triangle space corresponding to the target.

In addition, more bound gauges may be obtained according to the present invention when larger numbers of gauges are used.

Applicant wishes to note that in a typical example, a chemically active area of a target includes at least 10 binding points, as discussed hereinabove. 10 binding points provide 120 3-point configurations (120 = (10*9*8)/(1*2*3)).

Hence, it is well within the capabilities of one of skill in the art to identify the number of configurations recited in each of claims 47-49 by selecting an appropriate gauge set.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

M. The Examiner has stated that it is not clear whether the phrase "spatial configurations of moieties" recited in claim 26 differs from the spatial orientation of gauges.

Claim 26 has been canceled without prejudice, rendering moot the Examiner's rejection.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

N. The Examiner has stated that the phrase "at least said set of gauges" in claim 34 makes unclear how many sets are being used.

As described hereinabove, claim 34 has been amended to recite "said set of gauges" instead of "at least said set of gauges".

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

O. The Examiner has stated that the meaning of the term "control area" in claim 43 is not clear, and that the specification provides particular examples, but does not provide a standard for ascertaining the requisite composition.

Applicant believes that the instant application makes clear to anyone of skill in the art that a "control area" refers to an area on the target which can affect the behavior of the target when bound, but which is distinct from an area adapted to

engage the substrate of the target (e.g., the "biochemically active area" of claim 41, from which claim 43 depends). See, for example, page 28, lines 3-8, and Figure 1 therein, as well as page 49, lines 8-13, therein.

Applicant further believes that the distinction between an area adapted to engage a substrate and an area which is not adapted thusly would be clear to one of ordinary skill in the art, and that such distinctions are common practice in the art.

In view of the above, Applicant believes to have overcome the Examiner's rejection in this respect.

*35 U.S.C. §101 Rejection*

The Examiner has rejected claims 1-6, 8, 9, 14, 15, 24-35, 40-49, 54-56, 155, 156 and 158-163 under 35 U.S.C. §101 as being directed to non-statutory subject matter.

Specifically, the Examiner has stated that it is unclear whether the claimed invention is purely computational or *in vitro*, or a combination of the two, and assuming the method is computational, the claims do not recite any practical application of the method. The Examiner has further stated that the claims must set forth a practical application to produce a real-world result.

As discussed hereinabove, the claimed method includes experimental steps in addition to computational steps.

Applicant believes that the obtaining of information about a chemically active area of a target molecule using "real-world" assays of the target molecule, as recited in the claims, is clearly a real-world result.

Moreover, the Examiner has stated that the rejection is based on the assumption that the method is purely computational, and as this assumption is incorrect (as discussed hereinabove), Applicant believes that the Examiner's rejection is moot, and respectfully requests that the rejection be withdrawn.

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*35 U.S.C. §101/112, 1st Paragraph Rejection*

The Examiner has rejected claims 1-6, 8, 9, 14, 15, 24-36, 40-49, 54-56, 155, 156 and 158-163 under 35 U.S.C. §101 as lacking patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility.

The Examiner has further rejected claims 1-6, 8, 9, 14, 15, 24-36, 40-49, 54-56, 155, 156 and 158-163 under 35 U.S.C. §112, first paragraph, for not reasonably providing enablement for use of sets of indefinitely large amounts of gauges.

Specifically, the Examiner has stated that the claimed method is directed to use of simultaneous amount of a set of gauges to interact with the target molecule and evaluate its chemically active area, and that the specification does not teach how to use a large plurality (e.g., 100,000) of gauges interacting at the same time with the target molecule.

The Examiner has cited Fejzo et al. as teaching that using mixtures of large amounts of compounds simultaneously to analyze a target molecule is problematic.

Applicant wishes to note that the Examiner has not specifically stated any reasoning for the 35 U.S.C. §101 utility rejection. Applicant is therefore led to believe that the reasoning for the 35 U.S.C. §101 utility rejection is substantially identical to the reasoning for the 35 U.S.C. §112 rejection.

Applicant wishes to note further that the references by the Examiner to "simultaneous" use of a plurality of compounds appear to refer to a use of the plurality of compounds in a mixture, rather than merely using separate, unmixed compounds at the same time, as Fejzo et al. teaches that use of mixtures is problematic, but does not teach that using a plurality of unmixed compounds at the same time is problematic. Indeed, Fejzo et al. refers to high-throughput screening (see for example, the final sentence of the Abstract, and the 3rd paragraph of the Introduction of Fejzo et al.), a well-known technique allowing the measuring large numbers of compounds at the same time, wherein the compounds are separated from one another (typically in individual wells).

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In the interest of clarity, Applicant uses the term "simultaneous" hereinbelow to refer to the use of a plurality of compounds in a mixture, in accordance with the Examiner's use of the term.

In contrast to the Examiner's apparent understanding, the instant application does not in any way specify that the gauges must be used simultaneously.

On the contrary, the instant application describes known methods (e.g., automated parallel assay devices, DNA chips) for performing ***multiple*** assays for different gauges, which clearly indicates gauges being assayed separately and not simultaneously (see for example, page 30, line 22, to page 31, line 14, therein).

Furthermore, the instant application discloses that in ***some*** assays, a plurality of gauges may be assayed simultaneously (see page 32, lines 23-26, therein). This indicates that simultaneous measurement is not necessary. Moreover, the instant application does not suggest therein that the plurality of gauges being assayed simultaneously consists of the entire set of gauges which are to be assayed.

Furthermore, the purpose of the assaying in the claimed invention is to facilitate the obtaining of information about the target molecule via analysis of the assay results. Applicant believes that it would be readily apparent to one of skill in the art that the assay results would not have to be from a simultaneous assay of all gauges in order to be suitable for analysis, and hence, that no such simultaneous assay is required to carry out the claimed invention.

Thus, as the simultaneous assay of all gauges is not a necessary step of the claimed invention, Applicant believes that the Examiner's statements regarding the lack of enablement for such a simultaneous assay are moot.

In view of the above, Applicant believes to have overcome the Examiner's 35 U.S.C. §101 and 35 U.S.C. §112 rejections.

*35 U.S.C. §102 and 103 Rejections*

The Examiner has rejected claims 1-4, 26, 29-33, 36, 41-46, 155, 156, 158, 159 and 161 under 35 U.S.C. §102(b) as being anticipated by, or alternatively, under 35 U.S.C. §103(a) as being obvious over Fejzo et al.

Specifically, the Examiner has stated that Fejzo et al. teach a method of obtaining information about a chemically active area of a target molecule, comprising providing a diverse library of small molecules which are substantially rigid due to having aromatic rings, assaying the interaction of gauges with a target, and analyzing the assay results.

The Examiner has further stated that he has no way of testing whether the "gauges" of Fejzo et al. satisfy the claimed limitations, and that as the Office does not have the facilities for examining and comparing Applicant's gauges with the gauges of the prior art, the burden is on Applicant to show a novel or unobvious difference between the claimed gauges and the gauges of the prior art.

Applicant contends that Fejzo et al. clearly fails to teach:

a) a gauge set according to the claimed invention; and

b) analysis of assay results according to the claimed invention,

as discussed in detail below.

a) Gauge set

Claim 1 recites a set of gauges selected such that it spans at least 50% of a triangle space defining all possible triangular 3-point pharmacophores with distances in a range of 2-12 angstrom and with acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor and aromatic as possible binding point types at the vertices.

It would be apparent to one of skill in the art that the library taught by Fejzo et al. fails to meet this requirement by a wide margin, for the following reasons:

1. The library of Fejzo et al. is too small.

A ***single*** set of distances of a triangle allows the arrangement of the 6 possible binding types on the three triangle vertices in many different combinations, resulting in $6^3 = 216$ possible triangles. Moreover, spanning, as defined in claim 1, requires more than one gauge for each possible triangle.

In sharp contrast, Fejzo et al. teaches that 120 compounds or less are provided for each application of the method taught therein (see page 757, first paragraph, of Fejzo et al.)

Although gauges may comprise several triangular configurations, and a binding point may fit more than one binding type (e.g., hydrophobic and aromatic), it is clear that the 120 compounds taught by Fejzo et al. are far from being able to span ***all*** possible combinations of three triangle distances to an average extent of 50%.

Indeed, Applicant has analyzed the collections from MDL Inc. known as the ACD (Available Chemicals Directory) and SCD (Screening Compounds Directory), together representing ~3,000,000 commercially available compounds, and found that only for about 23% of triangle space were there 5 gauges (as opposed to six, as required according to the claims) capable of binding to each possible 3-point pharmacophore defined by that space, to a large extent due to the lack of suitable large molecules.

Moreover, Fejzo et al. teaches that the small library size is advantageous (see for example, paragraph bridging pages 760 and 761 of Fejzo et al.). Hence, Fejzo et al. provides no motivation to one of skill in the art to provide a considerably larger library.

2. The possible triangle distances in the library of Fejzo et al. are highly limited.

Of the frameworks taught by Fejzo et al. (see Figure 1 therein), those which are rigid are almost exclusively comprise a single aromatic rings or a fused bicyclic system. The possible distances allowed by molecules with such frameworks range only up to approximately 7 angstrom (e.g., the farthermost carbon atoms on naphthalene, an exemplary bicyclic compound taught by Fejzo et al., are approximately 5 angstrom apart), which represents only half of the range of 2-12 angstrom represented in the triangle space defined hereinabove.

Triangles wherein all three distances are in the lower half of the allowed range are limited to approximately $(1/2)^3 = 1/8$ of triangle space. Hence, the compounds of Fejzo et al. are limited to a very small portion of triangle space, and therefore can contribute very little to spanning the required 50% of triangle space.

In sharp contrast to the library of Fejzo et al., a gauge set according to the claimed invention would include many gauges with larger rigid scaffolds (e.g.,

tricyclic and tetracyclic compounds) so as to provide triangle distances throughout the range of 2-12 angstrom (see for example, pages 83-86, Section 14.3, of the instant application).

Moreover, the Fejzo et al. teaches that the small size of the molecules taught therein is advantageous (see for example, page 756, Results section, first sentence, in Fejzo et al.). Hence, Fejzo et al. provides no motivation to one of skill in the art to provide larger molecules.

3. The library of Fejzo et al. lacks diversity of binding points.

The aromatic frameworks used by Fejzo et al. to construct the library have few, if any, binding points attached thereto which are suitable for chemically binding to an acid, base, hydrophobic, hydrogen-bond donors, hydrogen-bond acceptors or aromatic. Few combinations of side chains are added to the frameworks, as only 132 compounds were generated from 32 frameworks (see page 757, first paragraph, and Figure 1, of Fejzo et al.). It therefore seems likely that a considerable fraction of the compounds in the library of Fejzo et al. fail to comprise a single triangular configuration suitable for binding a 3-point pharmacophore.

b) Analysis of assay results according to the claimed invention

The claimed invention includes analysis of assay results using triangular geometric substructures defined for the gauges. Such an analysis involves analyzing the structural features of the gauge (i.e., the binding points) in combination with the assay results, allowing one to obtain, for example, information regarding the structure of a chemically active area of a target molecule (e.g., a map of the active area).

In sharp contrast, Fejzo et al. neither teaches nor suggests using triangular geometric substructures in analysis. Indeed, the only information that the method of Fejzo et al. appears to provide is which compounds in the library bind to the target. Thus, for example, no structural information is obtained.

Applicant therefore believes that the claims are neither anticipated by, nor obvious over Fejzo et al., and are therefore allowable.

In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: June 3, 2008

Examiner: Michael L. BORIN
Group Art Unit: 1631
Attorney Docket: 35898

*Additional Amendments*

Applicant has chosen to further amend the claims in order to correct improve the clarity thereof and to correct clerical errors.

Claim 16 has been amended so as to recite "said configurations" instead of "configurations".

Claims 44-46 have been amended so as to recite "wherein said analyzing comprises" instead of "analyzing comprises".

Claim 162 has been amended so as to recite "said binding points of said gauges" instead of "the moieties".

Applicant contends that the above amendments are cosmetic and do not affect the scope of the claims.

*Examination of Generic and Non-Elected Claims*

In view of the amendments made to the claims and the arguments recited herein it is believed that the claims are allowable with respect to the elected species and hence examination of claims 1-25, 29-57, 102, 103, 155-159 and 161-163 in their generic context and with respect to all the species recited therein is respectfully requested.

In view of the above amendments and remarks it is respectfully submitted that claims 1-25, 29-57, 102, 103, 155-159 and 161-163 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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Date: December 3, 2008

***Enclosure:***

- Petition for Extension of Time (Three Months)